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KNOBBE MARTENS OLSON & BEAR LLP  
2040 MAIN STREET  
FOURTEENTH FLOOR  
IRVINE, CA 92614

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| EXAMINER |
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LUCAS, ZACHARIAH

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1648

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Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/087,013

Applicant(s)

SCHERF ET AL.

Examiner

Zachariah Lucas

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 15 April 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) 1-11, 22, 23, 25-31 and 34-55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 13-21, 24, 32 and 33 is/are rejected.
- 7) ☒ Claim(s) 12 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group IV, claims 12-21, 24, 32, and 33, drawn to CSA binding polypeptides of var proteins, including the FCR3.varCSA protein (also, protein of SEQ ID NO: 2) in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 1-11, 22, 23, 25-31, and 34-55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 8.

### *Information Disclosure Statement*

3. The information disclosure statement (IDS) submitted on September 27, 2002 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.
4. The following reference is in a foreign language accompanied by an English abstract. Due to this, the reference has been examined only to the extent of the disclosure in the abstract.  
  
Pouvelle et al., Med. Trop. 58: 187-98.

***Objections to the Application***

5. Claim 16 is objected to because of the following informalities: Claim 16 refers to uncharged amino acids. However, in describing the different types of amino acids on page 31, the description refers to polar neutral, but not to uncharged, amino acids. While the two would appear to be the same, the specification does not provide antecedent basis for the terminology used in the claims. It is suggested that the claim be amended to describe polar neutral, rather than uncharged, amino acids. Appropriate correction is required.

6. Claims 12, 18-21, and 24 are objected to because of the following informalities: these claims contain references to disclosed sequences using an incorrect format. Reference to a disclosed sequence should use the introductory term "SEQ ID NO:" followed by the number of the referenced sequence as provided in the applications sequence listing. Appropriate correction is required.

7. Claim 20 is objected to because of the following informalities: there is no article provided introducing the molecule that binds CSA. It is suggested that the applicant insert the article --a-- in front of the word "molecule" in line 3 of the claim. Appropriate correction is required.

***Claim Rejections - 35 USC § 101***

8. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

9. Claim 20 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. This claim reads on any protein with at least 80% homology to SEQ ID NO: 2. However, the claim does not require that the protein share any other characteristic of the protein (e.g. binding ability). In view of the fact that the claimed proteins include proteins that are 80% homologous to SEQ ID NO: 2, but share no other functional or other characteristics of the protein, the claim reads on embodiments for which no utility has been indicated or established. The claim is there for rejected for lack of utility.

Claim 20 is also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial or specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

10. Claim 24 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The claim reads, in part, on polypeptides encoded by the nucleic acid of claim 3, or by the nucleic acid of claim 4. Claim three describes a nucleic acid comprising SEQ ID NO: 1, or the complement thereto. Claim 4 describes a nucleic acid that comprises at least 9 consecutive amino acids of seq id 1 (shich encodes for SEQ ID NO: 2). The Applicant has not indicated any use for the polypeptide encoded by the complement of SEQ ID NO: 1.

Furthermore, the Applicant has not demonstrated a specific and substantial utility for trimers of SEQ ID NO: 2. The only utility provided for such peptides is the binding of

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chondroitin sulfate. However, the application discloses only large (>200 residues) polypeptides that are so capable. There are no examples of either trimers of SEQ ID NO: 2, or active regions of SEQ ID NO: 2 comprising a specific sequence of 3 residues from SEQ ID NO: 2, that can bind to CSA. Because the Applicant has not shown any trimer that is capable of binding CSA, and because no other utility has been established for peptides of at least residues, the claim is rejected for reading on material for which no utility has been ascribed.

***Claim Rejections - 35 USC § 112***

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims each describe a “purified or isolated protein of claim 12,” wherein at least one of a class of amino acids is replaced with a different amino acid. Claim 12 reads on a “purified or isolated protein comprising the sequence of SEQ ID NO: 2.” It is unclear whether the claims 13-17 read on a protein comprising both SEQ ID NO: 2, and another polypeptide or protein with the desired substitutions, or if the Applicant intended to claim a isolated or purified protein with a variant of SEQ ID NO: 2, wherein the variant has (e.g.) at least one amino acid substituted with another amino acid. It is noted that because claim 12 requires that the claimed protein comprises the sequence of SEQ ID NO: 2, and not a variant thereof, a dependant claim

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from this claim cannot properly “limit” the claim to such variants as appear to be described in the rejected claims.

13. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim describes a polypeptide comprising at least 3 consecutive residues of SEQ ID NO: 2, wherein the polypeptide “is found in molecule that binds to chondroitin sulfate A (CSA) that is at least 80% homologous to FCR3.varCSA.” The claim is indefinite because it is unclear whether the polypeptide, or the whole of the molecule that comprises it is at least 80% homologous to SEQ ID NO: 2.

Furthermore, as drafted, the claim appears to be requiring that the CSA to which the molecule comprising the claimed polypeptide binds, and not the molecule or polypeptide, are at least 80% homologous to FCR3.varCSA. Because chondroitin sulfate is not a protein, and therefore could not share 80% homology with SEQ ID NO: 2, the claim requires amendment to read more clearly.

14. Claims 19, 20, and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims reads on a polypeptide that is at least 80% to a sequence of SEQ ID NO: 2, or encoded by SEQ ID NO: 1. However, the sequence of SEQ ID NO: 2 (which is encoded by SEQ ID NO: 1) is referred to in claim 12 as a protein. It is therefore unclear whether the claims are describing a polypeptide wherein the polypeptide must

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be at least 80% identical to the full length of SEQ ID NO: 2, or if the polypeptides must be at least 80% identical to the portion of SEQ ID NO: 2 to which they correspond.

15. Claim 20 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim describes a polypeptide "wherein the polypeptide is at least 80% identical to the polypeptide having the amino acid sequence of SEQ ID NO: 1." This claim is indefinite because SEQ ID NO: 1 is a nucleic acid sequence, and not an amino acid sequence. It is therefore unclear whether the claim is to a polypeptide encoded by the sequence of SEQ ID NO: 1, or if the claim is intended to claim polynucleotides rather than polypeptides. Clarification is required.

16. Claim 21 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is unclear whether the claim is limited to the CIDR1 or DBL3 domains of SEQ ID NO: 2, or is intended to read on any CIDR1 or DBL3 domain of any var protein. Clarification is required.

17. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.



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18. Claims 18 and 24 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims describe polypeptides comprising at least 3 consecutive amino acids of SEQ ID NO: 2, wherein the polypeptide can bind to CSA. Claim 24 describes such a protein in its dependency from claim 6. The Applicant has claimed a genus of all polypeptides that both comprise at least 3 consecutive residues of SEQ ID NO: 2, and that can bind CSA.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed. In the present case, the Applicant has not provided such a disclosure. The Applicant has disclosed two regions of the protein (DBL3 and DBL7) that are capable of binding CSA. The Applicant has also disclosed

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two domains of other var proteins that can bind CSA (SEQ ID NOs: 9 and 11). Each of these regions is in excess of two hundred amino residues in length, and the application does not disclose that any trimer within the sequences that are, alone, capable of either binding CSA, or acting as markers for CSA binding activity.

As indicated above, the Applicant has not provided any working examples of the claimed inventions other than the five disclosed CSA binding domains (three from SEQ ID NO: 2, and two from other var proteins), or identified any correlation between trimers of SEQ ID NO: 2 generally, and the ability of the protein comprising them to bind to CSA. Because there is no such correlation, and because the Applicant has not provided any working examples to support the claim to the described genus, the claim is rejected for lack of written description support.

19. Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim describes polypeptides comprising at least 3 consecutive amino acids of SEQ ID NO: 2, wherein the polypeptide is found in a "molecule that binds to chondroitin sulfate (CSA) that is at least 80% homologous to FCR3.varCSA." Thus, for the purpose of this rejection, the claim is being interpreted as describing a genus of molecules comprising at least 3 consecutive residues of SEQ ID NO: 2, and wherein the molecule is capable of binding to CSA. This claim is rejected because the application has not provided written description support for claims to any protein of at least 80% homology to SEQ ID NO: 2 that is capable of binding to CSA.

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As indicated above, the application has disclosed two regions of the protein of SEQ ID NO: 2 that can bind to CSA. See, App., page 3 (disclosing that the regions coded DBL3 and DBL7 are able to bind CSA). Each of these two sequences has over 250 amino residues. Thus, the Applicant has indicated three CSA binding domains (DBL3, DBL7, and CIDR1) from the FCR.varCSA protein, two of which are related as DBL proteins. The Applicant has also disclosed two domains from other var proteins that bind CSA (page 3, lines 23-25). However, while the Applicant has provided these working examples of CSA binding domains, the specification has also disclosed several other related sequences from var proteins that are not capable of binding to CSA. More domains from the protein of SEQ ID NO: 2 are also disclosed, but are not identified as capable of binding CSA. See, page 3, lines 22-25 (disclosing domains of other var proteins), and Figure 1 (disclosing the various domains of the FCR.varCSA protein, only 3 of which are disclosed as binding to CSA). The Applicant has not disclosed how one skilled in the art could distinguish between the domains that do and do not bind CSA.

Further, the Applicant has not identified the residues or regions of these fragments that are necessary for CSA binding, or disclosed homologous sequences from which one in the art could identify such residues or regions. Thus, the Applicant has not shown that any protein with 80% homology to the protein of SEQ ID NO: 2, but that does not have the sequence of at least one of these three regions, is able to bind CSA. The Applicant has therefore not provided sufficient written description support for the claim to any molecule with at least 80% homology to SEQ ID NO: 2 that is able to bind to CSA.

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It is noted that the claims also require the presence of at least three consecutive residues of SEQ ID NO: 2. However, for the reasons described above with regards to claim 18, this limitation is not deemed sufficient to provide written description support for the rejected claim.

20. Claims 13-17, 18, 19, 20, and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for polypeptides comprising one of the DBL3, DBL7, or CIDR1 domains of the FCR.varCSA (residues 1279-1554 of SEQ ID NO: 2), does not reasonably provide enablement for polypeptides comprising any 3 consecutive amino acids of the SEQ ID NO: 2 wherein the polypeptide can bind CSA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims have either been described above, or relate to subject matter substantially equivalent to those claims already described.

The claims begin by claiming any polypeptide that shares at least 3 consecutive residues with SEQ ID NO: 2, and that binds to CSA, or that have the sequence of SEQ ID NO: 2, wherein at least one of a class of amino residues is substituted with another residue, but with no limits on the substitutions. However, as described above, the application does not disclose any trimer from SEQ ID NO: 2, that is either capable of, or a marker of, CSA binding. Nor does the Applicant disclose any variants from the original sequence that maintain its CSA binding ability.

The full length of SEQ ID NO: 2 comprises over 3500 residues. From this sequence, Applicant has disclosed three domains that are capable of binding CSA, each of which is over 250 residues in length. Pages 2-3. The Applicant has also disclosed two other domains from

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other var proteins that are able to bind CSA. Page 3. The Applicant has also disclosed several domains of both the FCR3.varCSA and other var proteins that are not able to bind CSA.

However, the Applicant has not identified any trimer from any of these sequences that is capable of binding to CSA, or that is indicative of such an ability. Nor has the Applicant been able to identify, even with the presence of these non-CSA binding examples, what residues or sequence characteristics are required for CSA binding.

In view of the teachings of the application identifying only three domains (of over 200 residues) that bind CSA, it is clear that there are a number of sequences, especially trimers, within SEQ ID NO: 2 that are not capable of binding to CSA. There is also a dearth of guidance that would lead those in the art towards such sequences. Further, as the application does not make clear what residues or sequences (other than the un-mutated versions of the DBL3, DBL7, and CIDR1 domains) are necessary for binding CSA, the Applicant has not provided any guidance as to what residues may be mutated without losing the ability of the protein to bind CSA. Given the potential scope of the claims, and the lack of any operative embodiments of or other guidance to, the claimed variants, the Applicant is not enabled for any protein comprising at least three consecutive residues of SEQ ID NO: 2, that is capable binding CSA.

Claim 19 further requires that the CSA binding protein, with at least 3 consecutive residues from SEQ ID NO: 2, must also share at least 80% homology with SEQ ID NO: 2. Claim 20 merely requires that the protein share 80% homology with SEQ ID NO: 2. However, the Applicant has not provided any examples of such proteins. It is known in the art the structures of var proteins have great variability, while, apparently, maintaining some form of binding ability. See e.g., WO 96/40766 (of record in the IDS filed September 27, 2002), page 7, first paragraph.

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However, although the structure of the proteins is open to variations, the effect of the variations is not known. For example, similarly structured var proteins (e.g. the various DBL2 proteins discussed on page 3 of the application) have different binding affinities. Furthermore, even with the presence of both CSA and non-CSA binding domain examples, the Applicant has not shown that one in the art can distinguish between such examples without first testing each variant for the ability to do so. In fact, in the reference by Roberts et al. (PNAS 96: 5198-202, submitted in the IDS), the prior art states, "Little is known about specific motifs that bind to CSA...." Id., page 5200, second paragraph. Thus, it becomes clear that those in the art would not, without further guidance, be able to make variants that maintain the capacity to bind CSA because they do not know the characteristics of CSA binding sequence necessary for the function.

While the art recognizes a great amount of variability may be found among the var protein sequences, the actual binding specificity of the proteins has also been shown to be variable. See, Scherf et al., EMBO Journal 17: 5418-26, at 5423, and Reeder et al., PNAS 96: 5198-2002, at 5201 (each of record in the IDS of September 27, 2002, and each disclosing relationships between certain forms of *P. falciparum* var proteins with different types of malaria infections). Thus, not all of the variants are able to bind CSA. Moreover, while the Applicant has shown sequences from other var proteins that can bind CSA (SEQ ID NOs: 9 and 11, App. page 3), these sequences share less homology than residues from var DBL sequences which are not disclosed as capable of binding CSA or indicated as isolated from maternal malarial infections (therefore likely to bind CSA). See, the attached sequence alignments of residues 1279-1554 with residues 1367-1650 from WO 96/40766 (about 40% homology, not shown to bind CSA), and with the sequences of SEQ ID NOs: 9 and 11 (about 30-35% homology, binds CSA). Given

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this lack of correlation between percent homology and CSA binding ability, and the lack of guidance by the Applicant showing what variants are likely to bind CSA, the Applicant is not enabled for any proteins of 80% homology to SEQ ID NO: 2 that are capable of binding CSA.

Given the number of potential variants, the unpredictability in the effect of the variations, and the lack of sufficient guidance to those in the art to determine which proteins will be able to bind to CSA, the applicant is not enabled for claims to any protein, with or without 80% homology to SEQ ID NO: 2, that can bind CSA. However, as the Applicant has provided examples of three domains from SEQ ID NO: 2 that are capable of CSA binding domains, the Applicant is enabled for such proteins that comprise at least one of the identified domains.

21. Claim 32 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This claim reads on a complex comprising "FCR3.varCSA and a ligand for FCR3.varCSA."

However, the application has identified only 1 ligand to the protein- CSA. However, the Applicant has also disclosed other binding domains of the protein for which no ligand has been identified. See, Figure 1 (identifying the domains of SEQ ID NO: 2). Nor is there any guidance as to what, if any, molecules are bound by these domains. Because the application does not disclose all of, or provide any indication as to what other ligands that CAS may be bound by the protein, the Applicant has not provided adequate written description for the claim language reading on any ligand to FCR3.varCSA.

22. Claim 33 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 33 reads, in relevant part, on isolated or purified biological complexes comprising fragments of FCR3.varCSA (SEQ ID NO: 2) and CSA or an analog thereof. However, the applicant has disclosed only three fragments of the protein of SEQ ID NO: 2 that are able to bind CSA. See e.g., the rejections of claims 18 and 19, supra. Thus, the Applicant has provided written description support for biological complexes of CSA with only those three fragments of the full-length protein, or fragments comprising at least one of those three domains. But there is not adequate written description support for claims to all fragments of FCR3.varCSA that can bind to CSA.

***Claim Rejections - 35 USC § 102***

23. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.



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24. Claims 13-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Sim et al., WO 96/40766. For the purposes of this rejection, these claims are being read as describing proteins that vary from SEQ ID NO: 2 by at least one amino acid substitution of a particular type.

However, none of the claims limits the number of substitutions or other mutations that may be made, or the amino acids that may be substituted. Nor do the claims set a required level of homology to SEQ ID NO: 2, or a function required by the variant protein. Thus, the claims read on any protein with any number of substitutions from SEQ ID NO: 2. Sim et al., teaches another *P. falciparum* protein. See, page 3, identifying SEQ ID NO: 14 as Genbank Accession number L42636, the NCBI printout of that Accession number showing that the protein is from *P. falciparum*. However, the protein disclosed therein does not appear to be capable of binding to CSA. Nonetheless, as can be seen by the sequence comparison between SEQ ID NO: 2 and the Sim protein (Result 5 for us-10-087-013-2.rag, pages 10-12), the protein disclosed therein varies from the protein of SEQ ID NO: 2 by at least one of each of the substitutions required in each of the rejected claims.

25. Claims 18 and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Reeder et al., PNAS 96: 5198-202 (of record in the IDS), in light of the associated DNA and amino acid sequences disclosed in GenBank Accession number AF134154 and AAD29126, respectively. These claims have been described above. Reeder discloses the identification of a cDNA encoding a *Plasmodium falciparum* erythrocyte surface receptor that binds to CSA. See, abstract. The cDNA and the encoded polypeptide of the isolated cDNA are disclosed in the two GenBank submissions above. As can be seen from the protein sequence, it shares, in several instances, at

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least three consecutive amino acids from SEQ ID NO: 2. See, e.g. residues 17-19, 102-106, 151-153, and 271-73, corresponding to residues 22-24, 110-113, 153-55, and 262-264, respectively, of SEQ ID NO: 2. The reference therefore anticipates claims 18 and 24.

26. Claims 18, 19, 20, and 24 are rejected under 35 U.S.C. 102(a) as being anticipated by Scherf et al., EMBO Journal, 17(18): 5418-26. Claim 15 describes a variants of SEQ ID NO: 2 wherein there are substitutions of in the protein of a polar amino acid for another polar amino acid. Claims 18 and 24 have been described above. Claims 19 and 20 are being interpreted as reading on polypeptides that must be at least 80% homologous to the portion of SEQ ID NO: 2 to which they correspond. The Scherf reference describes the isolation of a var protein of *P. falciparum* protein that binds to CSA. The reference discloses that the sequence of the protein may be found in GenBank Accession number AJ007940. The protein disclosed (as encoded by the DNA of this submission) both shares at least 3 amino acid residues with SEQ ID NO: 2, binds CSA (according to the disclosure of Scherf), has at least 80% homology to the residues 141-313 of SEQ ID NO: 2 (the portion to which the polypeptide corresponds). The reference therefore anticipates the identified claims.

### ***Conclusion***

27. The subject matter of claims 12 and 32 appear to be free of the prior art.

28. The following prior art references are made of record and are considered pertinent to applicant's disclosure. However, while relevant they are also not used as a basis for rejection for the stated reasons.

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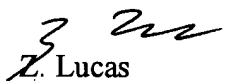
Gustafson, Stephan, U.S. Patent 5,817,644. This patent teaches a cell surface receptor protein that binds to hyaluronan and to CSA. However, because the reference does not disclose the sequence of the protein identified therein, it cannot be determined that the protein shares a common fragment of least 3 consecutive amino residues with the sequence of SEQ ID NO: 2.


Chen et al., J. Exp. Med. 187: 15-23 (of record in the IDS filed on September 27, 2002. This reference teaches a *P. falciparum* erythrocyte membrane protein which binds to glycosaminoglycans, but not, apparently to CSA. See, page 19.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

  
Z. Lucas  
Patent Examiner  
June 24, 2003

  
JAMES HOUSEL  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600  
6/30/03